ORANGE COUNTY REGULATORY AFFAIRS
Discussion Group

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November 29, 1999

Docket No. 99D-2873
Dockets Management Branch
Division of Management Systems and Policy
Office of Human Resources and Management Services
Food and Drug Administration
5630 Fishers Lane
Room 1061 (HFA-305)
Rockville, MD 20852

Re: Public Comment on *"Evidence Models for the Least Burdensome Means to Market"*

This letter provides comments prepared by an ad-hoc committee of the Orange County Regulatory Affairs Discussion Group (OCRA). We have reviewed the FDA draft guidance document, *"Evidence Models for the Least Burdensome Means to Market,"* which was released for comment on September 1, 1999.

OCRA Profile:

OCRA was organized in 1992 and incorporated in 1994. OCRA is chartered as a nonprofit educational group. OCRA's goals are to promote an atmosphere for open exchange of ideas and discussion for the Regulatory Affairs Professional from the Medical Device, Pharmaceutical, Biological, and Food and Cosmetic industries.

OCRA is truly a "grass roots" organization. Volunteers run our educational activities and OCRA does not have a full time paid staff. We currently have over 400 active members primarily from the Medical Device industry in Orange County; California. OCRA does not have any corporate members. Small companies with less than 50 employees employ approximately 40%-50% of our members. Although we are Orange County based, our meetings consistently draw from all over the West Coast region.

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Comments on "Least Burdensome Requirements" (LBR)

1) We commend FDA for not limiting the draft guidance to *effectiveness*, although the statute would have allowed you to do so. Our understanding is that the current guidance has extended the LBR concept to cover clinical studies for both *safety and effectiveness*.

2) FDA's view of LBR is narrower than the more comprehensive Trade Association Proposal (TAP) included with the draft guidance document. The guidance document addresses only the issues of clinical studies. As such, it might be more appropriate as guidance for an "agreement meeting" and not a "determination meeting" as to the least burdensome means of generating valid scientific evidence that demonstrate the device to be safe and effective for its intended use. OCRA supports the TAP model and believes that the scope of the LBR guidance should be expanded to include, as a minimum, the five levels of burden proposed by TAP (reference Section II, page 20 of the draft guidance document). We have redrafted the flow diagram provided in the guidance as Appendix 1; see our Attachment 1.

3) FDA has misinterpreted the TAP hierarchical (five level) model by implying each rung of the ladder is a sequential submission and review of available data, thereby adding delays. This need not be so. The hierarchical approach is a philosophy to be employed in making the determination as to the type of data necessary to answer the fundamental scientific issues of safety and effectiveness. It should not be an iterative process.

4) The TAP model should be expanded to include one additional level. This level should address the question: "*Is the device properly classified*?" In the U.S., the greatest burdens for product introduction are imposed on Class III/PMA products. Yet many of these products have been marketed for 1 O-20 years, and a large pool of safety and effectiveness data exists in the clinical literature and FDA's own records. OCRA believes that product reclassification (Class III to II) represents the most significant reduction of burden for any product introduction. Our redrafted Appendix 1, our Attachment 1, includes this additional level.

   FDA has made significant progress in reclassifying Class II products to Class I. However, this cannot be said about the reclassification of Class III products, although FDA recently proposed reclassification of 38 preamendment Class III devices into Class II. Petitions from trade and professional associations have triggered the majority of Class III products reclassified to date. FDA should develop a plan for agency reclassification of Class III products, similar to the Class II program.

   Medical Device Reporting (MDR) plays an important role in FDA enforcement activities; however, these data have not been utilized to trigger or support the reclassification of Class III products, Yet the MDR database represents a huge pool of product safety data for Class III products, typically exceeding a ten-year time span for a large number of devices. Although the MDR system does not capture all of the safety data for Class III products, these data can provide valuable indications regarding the safety of a device.

5) The scope of LBR should include the "Use of Data Relating to Premarket Approval, " which is described in Section 216 of FDAMA. FDA's ability to utilize data from PMAs

that are six years old could substantially reduce the burden of product approval for new devices, presuming that the devices raise no new issues of safety and efficacy when compared to existing commercially approved products. This provision can also be used to justify the reclassification of Class III devices.

6) The scope of LBR should include the process to modify an existing Class III device via 21 CFR 814.39(e), having to do with advisory opinions.

Specifically, under ¶ 814.39(e), FDA may prepare, among other actions, advisory opinions under ¶ 10.85 that make certain PMA supplements unnecessary. In these situations, there is the requirement that the PMA-related change be reported in a periodic report under ¶ 8 14.84 or in a 30-day PMA supplement.

Under ¶ 10.85, these advisory opinions can be in the form of FDA guidance issued under ¶ 18.90(b). We acknowledge and appreciate the increase in the number of guidance documents produced by FDA over the past several years. Many of these guidance documents are directed towards specific generic types of devices, including Class III devices subject to the PMA process. As more about a specific type of generic Class III device is understood by the industry and FDA, there are more areas where certain types of PMA supplements become a matter of routine. This is true especially when the applicant has already submitted and received approval of other PMA supplements of a similar nature.

Examples where this type of guidance would provide a least burdensome approach are the same as described for Class I and Class II devices in FDA's 510(k) Memorandum # K97-1. These include changes to:

- environmental specifications,
- performance specifications,
- dimensional specifications, and
- software and firmware where;

  the changes do not affect the indications for use, do not require clinical data to establish safety and effectiveness, and where the results of design validation do not raise new issues of safety and effectiveness.

These changes also include changes in packaging and expiration dating, and changes in sterilization where the changes do not affect the performance specification or decrease the Sterility Assurance Level. There are other examples included in FDA's 5 1 O(k) memorandum that also would be appropriate for Class III devices that could be described in an advisory opinion under ¶ 8 14.39(e).

We urge the Agency to make use of the fact that the design control provisions of the Quality System Regulation are well in place by now, and changes to devices that require PMA supplements should have been developed under design control. FDA has made the innovative "Special 5 1 O(k)" available for use by manufacturers for certain types of changes. We recognize and appreciate this least burdensome approach to obtaining 5 1 O(k) clearances for reserved Class I and Class II device changes. We propose that similar types of changes

would be appropriate for advisory opinion(s) under ¶ 814.39(e). These changes would not affect the intended use of the device, would not include a new technology, and would be subject to a certification that the change was developed in conformance to design controls under ¶ 820.30.

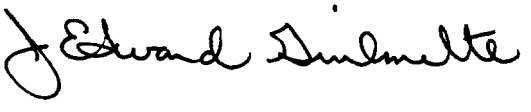
7) One implication of FDA's examples is that innovators must pave the way before less burdensome approaches to establishment of safety and effectiveness will be considered by FDA. This is a potential disincentive to innovation. Further, these examples suggest that FDA is not open to consideration of LBR other than randomized, controlled clinical studies for novel devices.

Conclusion:

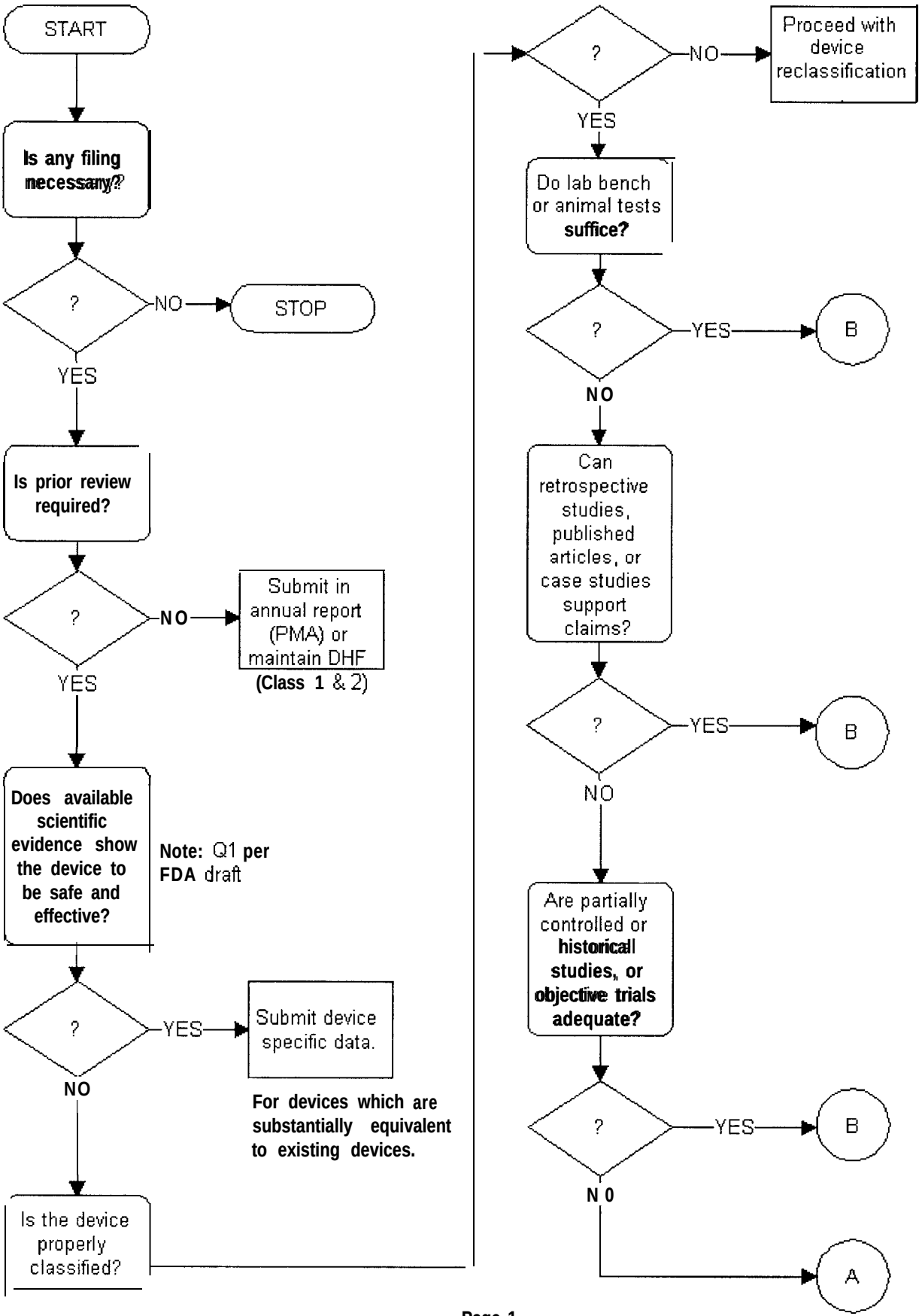
OCRA appreciates that FDA has published the September 1999 draft guidance document, and that the draft document applies to both safety and effectiveness. However, we believe that application of the document would increase, in many instances, the regulatory burden for manufacturers, instead of providing the least burdensome means to market. Furthermore, we believe that the scope of the document should be broadened to address additional topics of regulatory burden suggested in the TAP model instead of just focusing on clinical studies.

Thank you for the opportunity to provide these comments.

Sincerely,



OCRA ad-hoc committee, by
J. Edward Guilmette
President
OCRA


START
Is any filing necessary?
?
NO
STOP
YES
Is prior review required?
?
NO
Submit in annual report (PMA) or maintain DHF
(Class 1 & 2)
YES
Does available scientific evidence show the device to be safe and effective?
Note: Q1 per FDA draft
?
YES
Submit device specific data.
NO
For devices which are substantially equivalent to existing devices.
Is the device properly classified?
?
NO
Proceed with device reclassification
YES
Do lab bench or animal tests suffice?
?
YES
B
NO
Can retrospective studies, published articles, or case studies support claims?
?
YES
B
NO
Are partially controlled or historical studies, or objective trials adequate?
?
YES
B
NO
A

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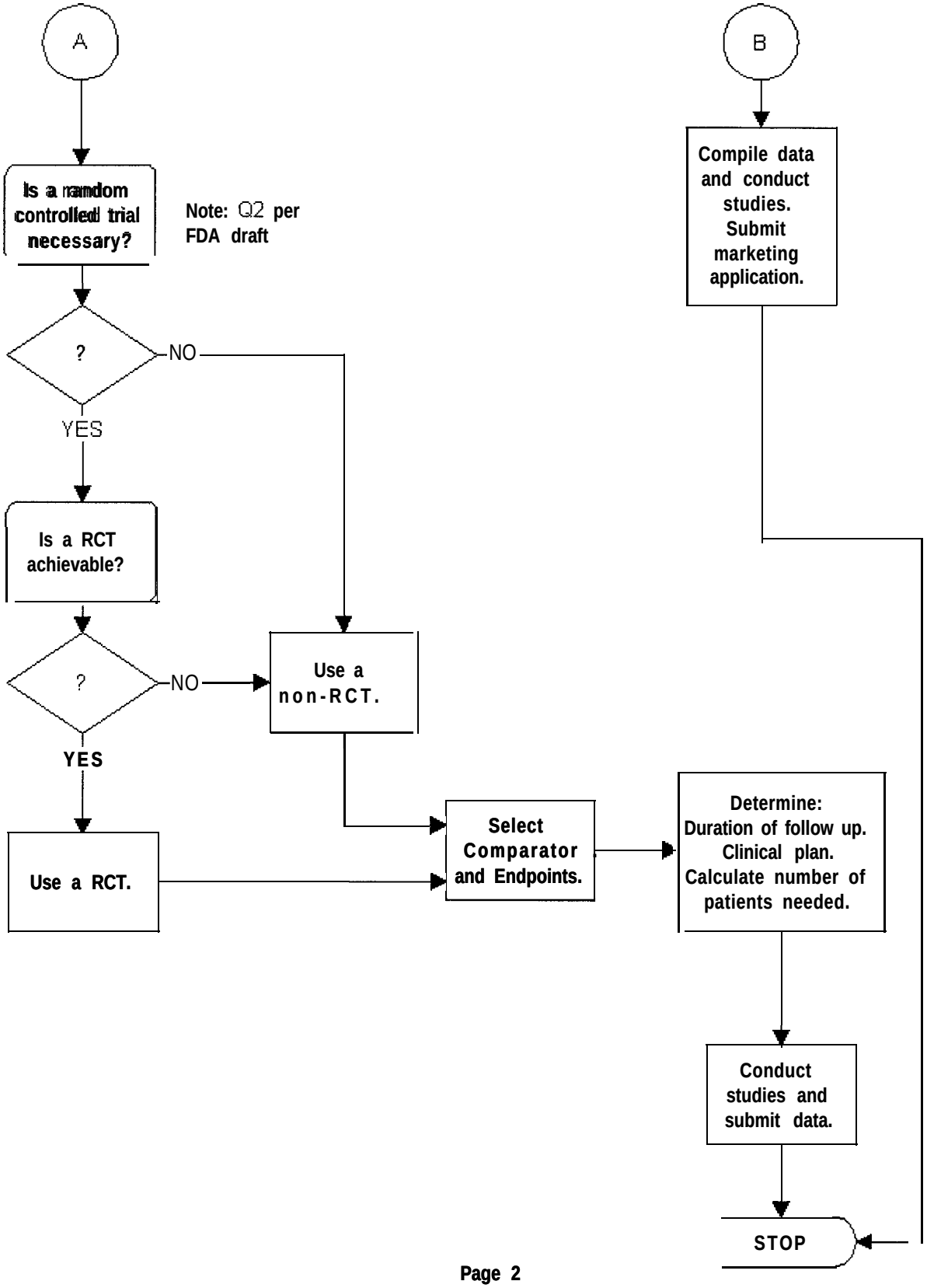

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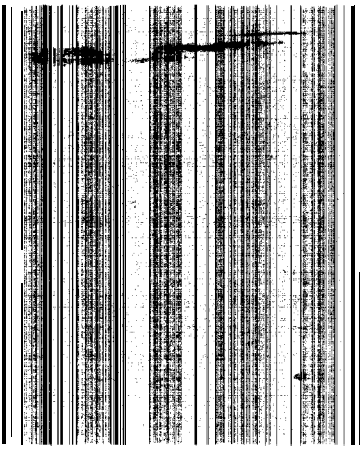

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